

Diethylphthalate

CAS #84-66-2

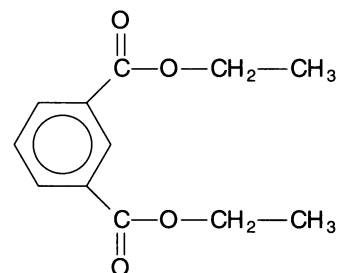
Swiss CD-1 mice, at 0.25, 1.25, and 2.5% in feed

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Diethylphthalate (DEP) was tested for reproductive toxicity in the standard Continuous Breeding design using Swiss CD-1 mice (Lamb et al., *Toxicol Appl Pharmacol* 88:255-269 [1987]). Data collected in the Task 1 dose-range-finding study (body weight, clinical signs, food and water consumptions) were used to select concentrations of 0.0, 0.25, 1.25, and 2.5% in feed for the main study. Feed consumption was not affected by the presence of DEP. These concentrations in feed gave calculated consumption estimates of 0.34, 1.77, and 3.64 g DEP/kg body weight/day.

DEP consumption had no adverse effect on the mean number of litters per pair, the number of live pups per litter, the viability of the pups, or pup body weight adjusted for litter size. In fact, the number of pups per litter was increased at the low and

middle doses by 32 and 14%, respectively. We attribute this to the fact that the value for the controls was approximately 25% below historical values for this strain.

Because there was no observable change in fertility or reproductive outcome, Task 3 (the crossover mating trial to determine the affected sex) was not conducted. The second generation was tested using the F₁ mice from the control and high dose groups.

There was no difference between these two groups in terms of body weights or viability of the F₁ pups at birth, weaning, or at the start of the week of mating (postnatal day 74 ± 10). All 20 pairs of mice mated in both groups, and 95% of those delivered live young (in both groups). The DEP litters had 14% fewer pups; viability and pup weight adjusted for litter size were unchanged.

After the F₂ pups were evaluated and discarded, the F₁ adults were killed and necropsied. Treated females weighed 8% less, while adjusted liver weight was increased by 28%. Treated males weighed 12% less than their respective controls, while their liver weight and prostate weight, both adjusted for body weight, were increased by 18 and 32%, respectively. Epididymal sperm concentration was reduced by 30%, while the percentage of motile sperm and the proportion of abnormal forms were unaffected by DEP.

In summary, DEP had no effect on F₀ reproductive performance, while producing moderate reproductive effects in the second generation in the presence of mild body weight gain inhibitions and moderate increases in liver weight.

DIETHYLPHthalate

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: PB85118636

Chemical: Diethylphthalate

CAS#: 84-66-2

Mode of exposure: Feed

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	0.25%	1.25%	2.5%
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, —	—, —
Kidney weight ^a		•	•	•
Liver weight ^a		•	•	•
Mortality		—, —	—, —	—, —
Feed consumption		—, —	—, —	—, —
Water consumption		•	•	•
Clinical signs		—, —	—, —	—, —

Reproductive toxicity				
̄ litters/pair		—	—	—
# live pups/litter; pup wt./litter		↑, —	↑, —	—, —
Cumulative days to litter		—	—	—
Absolute testis, epididymis weight ^a		•	•	•
Sex accessory gland weight ^a (prostate, seminal vesicle)		•	•	•
Epidid. sperm parameters (#, motility, morphology)		•	•	•
Estrous cycle length		•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F ₁ generation	Dose concentration →	•	•	2.5%
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		•	•	—, —
Mortality		•	•	•
Adult body weight		•	•	↓, ↓
Kidney weight ^a		•	•	•
Liver weight ^a		•	•	↑, ↑
Feed consumption		•	•	—, —
Water consumption		•	•	•
Clinical signs		•	•	•

Reproductive toxicity				
Fertility index		•	•	•
# live pups/litter; pup wt./litter		•	•	↓, —
Absolute testis, epididymis weight ^a		•	•	—, —
Sex accessory gland weight ^a (prostate, seminal vesicle)		•	•	↑, —
Epidid. sperm parameters (#, motility, morphology)		•	•	↓, —, —
Estrous cycle length		•	•	•

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	Unknown
NOAEL general toxicity:	Unknown
F ₁ more sensitive than F ₀ ?	Yes
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. ^aAdjusted for body weight.